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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,492	12/04/2001	Rango Dietrich	24826	6447

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NATH & ASSOCIATES PLLC
112 South West Street
Alexandria, VA 22314

EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 02/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,492	DIETRICH ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-15,18-20 and 33-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-15,18-20 and 33-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Amendment and Response after Non-Final Office Action, Applicant's Arguments/Remarks and the request for extension of time (1 month-granted), all filed 10/14/05 is acknowledged.

Upon further review and consideration, the previous Non-Final Office Action filed 06/16/05 has been withdrawn. The following are the new grounds of rejection:

Claims 11-15, 18-20 and 33-44 are pending in this action. Claim 13 has been amended. Claims 1-10, 16, 17, 21-32 and 45-47 have been cancelled. Claims 11-15, 18-20 and 33-44 are rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 11-15, 18-20 and 33-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benton *et al.* (U.S. Pat. No. 4,876,094) in view of Wong *et al.* (U.S. Pat. No. 6,120,803).

The instant invention is drawn to an active compound unit comprising an acid-labile active compound, wherein the acid-labile active compound in the active compound unit is selected from the group consisting of an acid-labile proton pump inhibitor, a salt of an acid-labile proton pump inhibitor with a base, and a hydrate of a salt of an acid-labile proton pump inhibitor with a base, and is present in a matrix made of a mixture comprising at least one fatty alcohol and at least one solid paraffin, wherein said active compound unit is a microsphere. The instant invention is also drawn to an active compound unit comprising an acid-labile active compound, wherein the acid-labile active compound in the active compound unit is selected from the group consisting of an acid-labile proton pump inhibitor, a salt of an acid-labile proton pump inhibitor with a base, and a hydrate of a salt of an acid-labile proton pump inhibitor with a base, and is present in a matrix made of a mixture comprising at least one fatty acid ester and at least one solid paraffin or in a matrix made of a mixture comprising at least one triglyceride and at least one solid paraffin, wherein said active compound unit is a microsphere.

Benton *et al.* ('094) teach a dual coated liquid dosage formulation comprising dosage form cores such as matrix beads/microspheres (which can be time release or controlled release devices) containing a therapeutically active compound over which there are applied two unique coatings. These two coatings enable dispersion of the coated dosage form cores in a liquid

carrier by imparting stability to the dosage form (see reference column 1, line 55 – col. 2, line 20).

Suitable controlled release type dosage form cores include controlled-release matrix beads/microspheres. The matrix beads/microspheres, typically are formed of a binder which is an insoluble material such as a soluble polymer or porous insoluble polymer or a wax which is intimately mixed with the therapeutically active compound (col. 3, lines 8-22).

Ingestible materials useful as a binder include waxes such as paraffin, higher fatty acids, esters of fatty acids such as glyceryl tristearate, cetyl palmitate, diglycol stearate, glyceryl myristate, triethylene glycol monostearate, higher fatty alcohols such as cetyl alcohol and stearyl alcohol and high molecular weight polyethylene glycols and mixtures thereof (col. 3, lines 23-36). The dosage form cores are microspheres or matrix beads coated with two materials. Most fats or glycerides include minor percentages of sterols, hydrocarbons, tocopherols and other non-glyceride constituents. The fats or glycerides can include mono-, di-, or triglycerides (col. 3, line 67 – col. 4, line 14).

Alternative to a homogenous mixture, a matrix bead/microsphere can be a core mixture of larger fragments of therapeutically active compound together with binder. In another variation, the binder can envelop a fragment of therapeutically active substance forming a microsphere, which is essentially a microcapsule. Assorted and various matrix bead and microsphere configurations are suitable provided they do not substantially exceed 1400 micron diameter (col. 3, lines 47-59).

The dual coated microspheres/matrix beads are preferred dosage forms and have a size range of 15-300 μm (col. 5, lines 48-54). This range meets Applicant's claimed range of 50-500

μm. The controlled release microspheres/matrix beads can be prepared by microencapsulation processes including prilling, pan coating, granulation fluidization processes and other processes (col. 5, lines 60-66).

Therapeutically active ingredients are taught at column 6, lines 41-50. Active ingredients taught include theophylline, antihistamines, cold formulations, analgesics, amino acid supplements, vitamins (*i.e.*, vitamin C), geriatric drugs, antidepressants and the like.

Benton *et al.* do not teach an active compound being an acid-labile proton pump inhibitor or a salt of an acid-labile proton pump inhibitor with a base or a hydrate of a salt of an acid-labile proton pump inhibitor with a base.

Wong *et al.* ('803) teach a prolonged release active agent dosage formulation adapted for gastric retention. The dosage formulation includes coated microspheres of an active agent or microspheres of an active agent and adjuvant, wherein especially suitable active agents are active agents for the localized treatment of gastric acidity and gastrointestinal disorders (*i.e.*, duodenal/peptic ulcers; chronic gastritis) such as omeprazole and lansoprazole (see reference column 18, line 1 – col. 20, line 12). Additional active agents include proteins, steroids, antidepressants, analgesics, antihistamines and the like.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the proton pump inhibiting active compounds, such as omeprazole or lansoprazole taught by Wong *et al.* within the dosage formulation of Benton *et al.*, because Wong *et al.* teach that the active agents (*i.e.*, omeprazole, lansoprazole) are especially useful in their invention for the localized treatment of gastric acidity and gastrointestinal disorders, such as

duodenal ulcers, peptic ulcers and chronic gastritis. The expected result would be an improved and effective proton pump inhibiting dosage formulation for the treatment of gastrointestinal disorders and conditions.

Claims 11-15, 18-20 and 33-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steber (U.S. Pat. No. 5,213,810) in view of Wong *et al.* (U.S. Pat. No. 6,120,803).

The instant invention is drawn to an active compound unit comprising an acid-labile active compound, wherein the acid-labile active compound in the active compound unit is selected from the group consisting of an acid-labile proton pump inhibitor, a salt of an acid-labile proton pump inhibitor with a base, and a hydrate of a salt of an acid-labile proton pump inhibitor with a base, and is present in a matrix made of a mixture comprising at least one fatty alcohol and at least one solid paraffin, wherein said active compound unit is a microsphere. The instant invention is also drawn to an active compound unit comprising an acid-labile active compound, wherein the acid-labile active compound in the active compound unit is selected from the group consisting of an acid-labile proton pump inhibitor, a salt of an acid-labile proton pump inhibitor with a base, and a hydrate of a salt of an acid-labile proton pump inhibitor with a base, and is present in a matrix made of a mixture comprising at least one fatty acid ester and at least one solid paraffin or in a matrix made of a mixture comprising at least one triglyceride and at least one solid paraffin, wherein said active compound unit is a microsphere.

Steber ('810) teaches stable microsphere compositions and methods of making microsphere compositions containing a fat, wax or mixture thereof; a biologically active protein, peptide or polypeptide; and an oil, semi-soft fat, fatty acid derivative or mixture thereof (see Abstract and Claims).

A preferred embodiment involves the incorporation of the biologically active protein, peptide or polypeptide in fat or wax microspheres and oil or semi-soft fat which may optionally also contain some or all of the excipients described in column 4 (see col. 4, lines 43-57).

The microspheres, preferably fat microspheres, may be up to 1,000 microns in diameter, with a weight average size range of 25 microns to 300 microns being preferred (col. 4, lines 43-57). This range meets Applicant's claimed range of 50-500 μm.

The addition of a small amount of oil, semi-soft fat and/or fatty acid derivative to the mixture of fats and/or waxes and the biologically active protein, peptide or polypeptide before prilling allows for an increased stability microsphere composition (column 2, lines 5-26).

Waxes and fats suitable for the invention include hydrocarbons, esters of fatty acids and alcohols. Included are saturated or unsaturated long chain fatty acids, alcohols, esters, salts, ethers or mixtures thereof (col. 2, lines 39-58).

Suitable waxes taught include fossil or earth waxes such as ozocerite and petroleum waxes such as paraffin, microcrystalline (col. 2, lines 60-68).

Fats include glyceryl esters of higher fatty acids such as stearic and palmitic. The fat is preferably composed of mono-, di-, or triglyceryl esters of long chain fatty acids. The mono-, di-, or triglycerides are composed predominantly of stearates, palmitates, laureates, linoleates,

oleates and residues or mixtures thereof. Glyceryl tristearate is a most preferred fat (col. 3, lines 6-68).

The microspheres of the invention may be prepared by incorporating the active ingredient having the desired particle size, and other excipients with a molten fat, wax or mixture thereof, admixing the oil, semi-soft fat and/or fatty acid derivatives and then forming microspheres of the resulting mixture by a variety of techniques include atomizing or prilling the mixture or by processing the mixture of ingredients of fat, wax or mixture thereof mechanically and cooling, for example utilizing a centrifugal disc. Alternatively, the mixture of active ingredients, excipients, fat, waxes and mixtures thereof and oil may be cooled to give a solid which may then be processed by procedures such as milling, grinding and the like (col. 5, lines 52-65).

According to Steber, mixtures of hard fats with liquid fats when melt blended and spray atomized to form prills or microspheres show accelerated transformation of alpha to beta crystal at room temperature and show markedly improved physical stability and exceptional attributes (col. 6, lines 3-15).

Active ingredients taught by Steber are biologically active protein, peptide or polypeptide.

Steber does not teach an active compound being an acid-labile proton pump inhibitor or a salt of an acid-labile proton pump inhibitor with a base or a hydrate of a salt of an acid-labile proton pump inhibitor with a base.

Wong *et al.* ('803) teach a prolonged release active agent dosage formulation adapted for gastric retention. The dosage formulation includes coated microspheres of an active agent or

microspheres of an active agent and adjuvant, wherein especially suitable active agents are active agents for the localized treatment of gastric acidity and gastrointestinal disorders (*i.e.*, duodenal/peptic ulcers; chronic gastritis) such as omeprazole and lansoprazole (see reference column 18, line 1 – col. 20, line 12). Additional active agents include proteins, steroids, antidepressants, analgesics, antihistamines and the like.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the proton pump inhibiting active compounds, such as omeprazole or lansoprazole taught by Wong *et al.* within the dosage formulation of Steber. One of ordinary skill in the art would be motivated to do so because Wong *et al.* teach active agents that include omeprazole, lansoprazole and teach that these active agents (*i.e.*, omeprazole, lansoprazole) are especially useful in their invention for the localized treatment of gastric acidity and gastrointestinal disorders, such as duodenal ulcers, peptic ulcers and chronic gastritis. The expected result would be an improved and effective proton pump inhibiting dosage formulation for treating an array of gastrointestinal disorders.

Response to Arguments

Applicant's arguments, see Applicant's Arguments/Response, filed 10/14/05, with respect to the 35 U.S.C. 103(a) rejections of claims 11-15, 18-20 and 33-44 over the combinations of Akiyama et al. (U.S. Pat. No.5,948,773); Shell et al. (U.S. Pat. No. 5,972,389); Matoba et al. (U.S. Pat. No. 5,456,920) & Sawhney et al. (U.S. Pat. No. 6,632,457) have been fully considered and are persuasive. The Non-Finality of the rejections has been withdrawn.

The 35 U.S.C. 112, 2nd paragraph rejection for claim 13 has also been withdrawn, by virtue of Applicant's amendment of deletion of the term 'further' in claim 13.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday from 8:00A.M. to 5:30P.M., alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Humera N. Sheikh Humera N. Sheikh

Patent Examiner TC-1600

Art Unit 1615

January 30, 2006

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